REMARKS

I. Status of Claims

Claims 31-38, 40-54, and 56-66 are pending in this application and were considered by the Board of Patent Appeals and Interferences ("the Board") in Appeal No. 2005-0593 heard March 15, 2005. No amendments herein.

II. Rejections under 35 U.S.C. § 103

In the Board's Decision on Appeal dated March 31, 2005, the rejection under 35 U.S.C. § 103(a) of claims 31-38, 40-54, and 56-66 over Hahn in view of Wahl or Hahn in view of Williamson or Hahn in view of Williamson and Wahl was reversed, but the Board remanded the application to the Examiner to consider the applicability of U.S. Patent No. 5,847,003 to Ptchelintsev et al. ("the '003 patent") to the pending claims. *See* Decision on Appeal dated March 31, 2005, at page 7. Subsequent to the Board's decision, the Office issued an Office Action on July 29, 2005, rejecting claims 31-38, 40-45, and 56-66 under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 5,951,990 to Ptchelintsev ("the '990 patent") or the '003 patent, and over the combination of U.S. Patent No. 5,449,688 to Wahl et al. ("the '688 patent") in view of either the '990 patent or the '003 patent. Office Action at pages 2 and 4. Applicant respectfully disagrees and traverses each of the rejections for the following reasons.

First, Applicant points out that, as recognized by the Board, the present application is based on PCT/FR96/00296, filed February 26, 1996. Applicant also notes that an English language translation of PCT/FR96/00296 (i.e., WO 96/26711) was filed in the U.S. Patent and Trademark Office on August 27, 1997, concurrently with the entry

of this application into the national stage. This translation was accepted by the U.S. Patent and Trademark Office, as evidence by the Notification of Acceptance of Application under 35 U.S.C. § 371 and 37 C.F.R. 1.494 or 1.495 mailed on October 30, 1997. In Table 1 below, Applicant points out the support in the English language translation of PCT/FR96/00296 for each element of claims 31-38, 40-54, and 56-66, which establishes Applicant's entitlement to the benefit of the filing date of the international application, i.e., February 26, 1996 for each element of each claim. *See* 35 U.S.C. § 363 and PCT Article 11(3).

TABLE 1

Claim	Disclosure in the English Translation of PCT/FR96/00296
31. A cosmetic or pharmaceutical composition, said composition comprising, in a cosmetically or pharmaceutically acceptable medium, at least one cosmetic or pharmaceutical product capable of causing a cutaneous irritant effect, and at least one topically applied nitric oxide synthase inhibitor, wherein said at least one topically applied nitric oxide synthase inhibitor is present in an amount effective to reduce the cutaneous irritant effect of said at least one cosmetic or pharmaceutical product.	Page 4 - "[T]he present invention also relates to composition for topical, cosmetic or pharmaceutical use characterized in that it comprises, in a cosmetically or pharmaceutically acceptable medium, an effective quantity of at least one NO-synthase inhibitor and at least one product capable of causing cutaneous irritation." Page 5 - "[T]he quantity of the product capable of causing a cutaneous irritation may therefore correspond to a quantity which is sufficient to cause a cutaneous irritation if it was used alone (without the NO-synthase inhibitor)."
32. A composition according to claim 31, wherein said pharmaceutical composition is a dermatological composition.	Page 4 - "The pharmaceutical composition is preferably a dermatological composition."

Claim	Disclosure in the English Translation of PCT/FR96/00296
33. A composition according to claim 31, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-6}% to 10% by weight relative to the total weight of the composition.	Pages 4 and 5 - "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration by weight of between 10^{-6}% and 10% of the total weight of the composition and preferably between 10^{-4}% and 1% of the total weight of the composition."
34. A composition according to claim 33, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-4}% to 1% by weight relative to the total weight of the composition.	Pages 4 and 5 - "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration by weight of between 10^{-6}% and 10% of the total weight of the composition and preferably between 10^{-4}% and 1% of the total weight of the composition."
35. A composition according to claim 31, wherein said at least one cosmetic or pharmaceutical product is a preservative, a surfactant, a perfume, a solvent, or a propellent.	Page 5 – "Thus, even the products which are considered to be inert in a cosmetic or pharmaceutical, more particularly dermatological, composition may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, such as in particular preservatives, surfactants, perfumes, solvents or propellants."
36. A composition according to claim 35, wherein said at least one cosmetic or pharmaceutical product is a sunscreen, an α-hydroxy acid, a β-hydroxy acid, an α-keto acid, a β-keto acid, a retinoid, an anthralin, an anthranoid, a peroxide, minoxidil or one of its derivatives, a lithium salt, an antiproliferative agent, vitamin D or one of its derivatives, vitamin B9 or one of its derivatives, a hair dye, a hair colorant,	Pages 5 and 6 – "Accordingly, products considered as active agents in cosmetic or pharmaceutical compositions may exhibit an irritant character . . . such as especially some sunscreens, α-hydroxy acids . . . β-hydroxy acids . . . α-keto acids, β-keto acids, retinoids . . . anthralins . . . anthranoids . . . peroxides . . . minoxidil and its derivatives . . . lithium salts, antiproliferative agents . . . vitamin D and

Claim	Disclosure in the English Translation of PCT/FR96/00296
capsaicin, a perfuming alcoholic solution, an antiperspirant, a depilatory waving active agent, a permanent waving active agent, a depigmenting agent, an antilouse active agent, a detergent, or a propigmenting agent.	its derivatives, hair dyes or colorants . . . perfuming alcoholic solutions, antiperspirants . . . depilatory or permanent waving active agents, depigmenting agents . . . capsaicin . . . antilouse active agents . . . ionic and nonionic detergent agents and propigmenting agents."
37. A composition according to claim 36, wherein said β-hydroxy acid is salicylic acid or one of its derivatives.	Page 5 – "β-hydroxy acids (salicylic acid and its derivatives) . . . ."
38. A composition according to claim 36, wherein said at least one cosmetic or pharmaceutical product is a retinoid.	Page 6 – "Among these products with a secondary irritant effect, the invention relates more particularly to retinoids."
40. A composition according to claim 36, wherein said vitamin D or one of its derivatives is vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3, calcipotriol, 1,24-diOH vitamin D_3, 24,25-diOH vitamin D_3, 1-OH vitamin D_2, or 1,24-diOH vitamin D_2.	Pages 6 and 7 - "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2."
41. A composition according to claim 40, wherein said 1,24-diOH vitamin D_3 is tacalcitol.	Pages 6 and 7 - "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2."
42. A composition according to claim 37, wherein said salicylic acid derivative is 5-n-octanoylsalicylic acid, 5-n-	Page 7 – "Among the salicylic derivatives, there may be mentioned more particularly 5-n-octanoylsalicylic acid and 5-n-

Claim	Disclosure in the English Translation of PCT/FR96/00296
dodecanoylsalicylic acid, or one of their esters.	dodecanoylsalicylic acid or their esters."
43. A composition according to claim 31, wherein said at least one nitric oxide synthase inhibitor is an inhibitor of constitutive nitric oxide synthase.	Page 7 - "The NO-synthase inhibitors are, according to the invention, products which make it possible in situ, in man, to partially or even completely inhibit the synthesis of nitrogen monoxide (NO). This enzyme exists in two forms, the constitutive form and the inducible form (Medecine/Sciences, 1992, 8, pp. 843-845)."
44. A composition according to claim 43, wherein said inhibitor of constitutive nitric oxide synthase is an inhibitor of endothelial nitric oxide synthase.	Pages 7 and 8 - "Among these inhibitors of constitutive NO-synthase, the inhibitors of endolethlial NO-synthase are preferred."
45. A composition according to claim 43, wherein said at least one nitric oxide synthase inhibitor is N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, N^G-amino-L-arginine, or N^G,N^G-dimethylarginine.	Page 8 - "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen."
46. A composition according to claim 45, wherein said at least one nitric oxide synthase inhibitor is the methyl ester of N^G-nitro-L-arginine, N^G,N^G-dimethylarginine, N^G-nitro-L-arginine or N^G-monomethyl-L-arginine.	Page 8 - "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-

Claim	Disclosure in the English Translation of PCT/FR96/00296
	dimethylarginine, aminoguanidine, canavanine and ebselen."
47. A composition according to claim 31, wherein said composition is formulated in order to be applied topically to the skin, the scalp, or the mucous membranes.	Page 9 - "By the topical route, direct application to the skin, the scalp, the nails or the mucous membranes is preferred."
48. A method of reducing the cutaneous irritant effect of a topically applied cosmetic or pharmaceutical composition containing at least one cosmetic or pharmaceutical product capable of having an irritant character on the skin, the scalp, the nails, or the mucous membranes, said method comprising applying said cosmetic or pharmaceutical product to said skin, scalp, nails, or mucous membranes, wherein said cosmetic or pharmaceutical composition further comprises at least one nitric oxide synthase inhibitor in an amount effective to reduce the cutaneous irritant effect of said at least one cosmetic or pharmaceutical product.	Page 3 - 'Now, the Applicant has discovered that the NO-synthase inhibitors make it possible to limit, or even suppress, the irritant character of these products." Page 3 - "The present invention also relates to a process of cosmetic treatment, characterized in that it uses the cosmetic composition according to the invention." Page 18 - "Preferably, the process of cosmetic treatment consists in applying to the skin, scalp and/or the mucous membranes a composition as described above."
49. A method according to claim 48, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-6}% to 10% by weight relative to the total weight of the composition.	Pages 4 and 5 - "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration by weight of between 10^{-6}% and 10% of the total weight of the composition and preferably between 10^{-4}% and 1% of the total weight of the composition."
50. A method according to claim 49, wherein said at least one nitric oxide synthase inhibitor is present in a	Pages 4 and 5 - "However, by way of illustration, a composition according to the invention comprises in general at least one

Claim	Disclosure in the English Translation of PCT/FR96/00296
concentration ranging from 10^{-4}% to 1% by weight relative to the total weight of the composition.	NO-synthase inhibitor at a concentration by weight of between 10^{-6}% and 10% of the total weight of the composition and preferably between 10^{-4}% and 1% of the total weight of the composition."
51. A method according to claim 50, wherein said at least one cosmetic or pharmaceutical product is a preservative, a surfactant, perfume, a solvent, or a propellent.	Page 5 – "Thus, even the products which are considered to be inert in a cosmetic or pharmaceutical, more particularly dermatological, composition may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, such as in particular preservatives, surfactants, perfumes, solvents or propellants."
52. A method according to claim 48, wherein said at least one cosmetic or pharmaceutical product is a sunscreen, an α-hydroxy acid, a β-hydroxy acid, an α-keto acid, a β-keto acid, a retinoid, an anthralin, an anthranoid, a peroxide, minoxidil or one of its derivatives, a lithium salt, an antiproliferative agent, vitamin D or one of its derivatives, vitamin B9 or one of its derivatives, a hair dye, a hair colorant, capsaicin, a perfuming alcoholic solution, an antiperspirant, a depilatory waving active agent, a permanent waving active agent, a depigmenting agent, an antilouse active agent, a detergent, or a propigmenting agent.	Pages 5 and 6 – "Accordingly, products considered as active agents in cosmetic or pharmaceutical compositions may exhibit an irritant character . . . such as especially some sunscreens, α-hydroxy acids . . . β-hydroxy acids . . . α-keto acids, β-keto acids, retinoids . . . anthralins . . . anthranoids . . . peroxides . . . minoxidil and its derivatives . . . lithium salts, antiproliferative agents . . . vitamin D and its derivatives, hair dyes or colorants . . . perfuming alcoholic solutions, antiperspirants . . . depilatory or permanent waving active agents, depigmenting agents . . . capsaicin . . . antilouse active agents . . . ionic and nonionic detergent agents and propigmenting agents."
53. A method according to claim 52, wherein said β-hydroxy acid is salicylic acid or one of its derivatives.	Page 5 – "β-hydroxy acids (salicylic acid and its derivatives) . . . ."

Claim	Disclosure in the English Translation of PCT/FR96/00296
54. A method according to claim 52, wherein said at least one cosmetic or pharmaceutical product is a retinoid.	Page 6 – "Among these products with a secondary irritant effect, the invention relates more particularly to retinoids."
56. A method according to claim 52, wherein said vitamin D or one of its derivatives is vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3, calcipotriol, 1,24-diOH vitamin D_3, 24,25-diOH vitamin D_3, 1-OH vitamin D_2, or 1,24-diOH vitamin D_2.	Pages 6 and 7 - "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2."
57. A method according to claim 56, wherein said 1,24-diOH vitamin D_3 is tacalcitol.	Pages 6 and 7 - "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2."
58. A method according to claim 53, wherein said salicylic acid derivative is 5-n-octanoylsalicylic acid, 5-n-dodecanoylsalicylic acid, or one of their esters.	Page 7 – "Among the salicylic derivatives, there may be mentioned more particularly 5-n-octanoylsalicylic acid and 5-n-dodecanoylsalicylic acid or their esters."
59. A method according to claim 48, wherein said at least one nitric oxide synthase inhibitor is an inhibitor of constitutive nitric oxide synthase.	Page 7 - "The NO-synthase inhibitors are, according to the invention, products which make it possible in situ, in man, to partially or even completely inhibit the synthesis of nitrogen monoxide (NO). This enzyme exists in two forms, the constitutive form and the inducible form (Medecine/Sciences, 1992, 8, pp. 843-845)."

Claim	Disclosure in the English Translation of PCT/FR96/00296
60. A method according to claim 59, wherein said inhibitor of constitutive nitric oxide synthase is an inhibitor of endothelial nitric oxide synthase.	Pages 7 and 8 - "Among these inhibitors of constitutive NO-synthase, the inhibitors of endolethlial NO-synthase are preferred."
61. A method according to claim 59, wherein said at least one nitric oxide synthase inhibitor of N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, N^G-amino-L-arginine, or N^G,N^G-dimethylarginine.	Page 8 - "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen."
62. A method according to claim 61, wherein said at least one nitric oxide synthase inhibitor is the methyl ester of N^G-nitro-L-arginine, N^G,N^G-dimethylarginine, N^G-nitro-L-arginine, or N^G-monomethyl-L-arginine.	Page 8 - "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen."
63. A process for the cosmetic treatment of the skin, the scalp, the nails, or the mucous membranes, said process comprising applying a cosmetic composition according to Claim 31 to said skin, scalp, nails, or mucous membranes.	Page 9 - "By the topical route, direct application to the skin, the scalp, the nails or the mucous membranes is preferred."
64. A process for the pharmaceutical	Page 4 - "The pharmaceutical composition

Claim	Disclosure in the English Translation of PCT/FR96/00296
treatment of the skin, the scalp, the nails, or the mucous membranes, said process comprising applying a pharmaceutical composition according to Claim 31 to said skin, scalp, nails, or mucous membranes.	is preferably a dermatological composition." Page 9 - "By the topical route, direct application to the skin, the scalp, the nails or the mucous membranes is preferred."
65. A composition according to claim 38, wherein said retinoid is all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester.	Page 13 - "Among the retinoids, there may be mentioned more particularly all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid sold under the name Adapalène™ by the company Galderma, Taxarotène™ sold by the company Allergan."
66. A method according to claim 54, wherein said retinoid is all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester.	Page 13 - "Among the retinoids, there may be mentioned more particularly all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid sold under the name Adapalène™ by the company Galderma, Taxarotène™ sold by the company Allergan."

With respect to the '003 patent, Applicant notes that the patent's earliest effective filing date is June 4, 1996. *See* M.P.E.P. § 706.02(a). This date is after the filing date of the PCT application which this application is a National stage of, i.e., February 26,

1996. Accordingly, since Applicant has demonstrated in Table 1 that all elements of all claims of the present application are supported in the PCT application, the '003 patent is not prior art to the present application, and as such, Applicant respectfully requests the withdrawal of the rejection of claims 31-38, 40-54, and 56-66 under Section 103 over the '003 patent.

In addition, Applicant submits herewith a certified English translation of French Application No. 95/02,267 filed on February 27, 1995, which Applicant claims the benefit of priority to under 35 U.S.C § 119. As demonstrated below in Table 2, which is a comparison with the English translation of French Application No. 95/02,267 showing that at least some of the pending claims are fully supported in French Application No. 95/02,267 and as such, claims 31-42, 45-58, and 61-66 are also entitled to the benefit of the filing date of the French Application, i.e., February 27, 1995. The earliest effective filing of the '990 patent is May 15, 1995, which is after this date. Thus, neither the '990 patent nor the '003 patent are effective as prior art against these claims for this additional reason.

TABLE 2

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
31. A cosmetic or pharmaceutical composition, said composition comprising, in a cosmetically or pharmaceutically acceptable medium, at least one cosmetic or pharmaceutical product capable of causing a cutaneous irritant effect, and	Page 4 – "The present invention also relates to a cosmetic composition comprising an effective quantity of at least one NO-synthase inhibitor, in a cosmetically or pharmaceutically acceptable medium." Page 8 – "Thus, according to a particular

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
at least one topically applied nitric oxide synthase inhibitor, wherein said at least one topically applied nitric oxide synthase inhibitor is present in an amount effective to reduce the cutaneous irritant effect of said at least one cosmetic or pharmaceutical product.	embodiment of the composition according to the invention, the cosmetic or pharmaceutical composition is characterized in that it comprises an effective quantity of at least one NO-synthase inhibitor and a quantity of a product capable of causing skin irritations when it is applied topically." Page 8 – "Preferably, the quantity of the product capable of causing skin irritation is sufficient to cause skin irritation." *See* Claims 16,19 and 20.
32. A composition according to claim 31, wherein said pharmaceutical composition is a dermatological composition.	Page 4 – "The pharmaceutical composition is preferably a dermatological composition." *See* Claim 17.
33. A composition according to claim 31, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-6}% to 10% by weight relative to the total weight of the composition.	Pages 4 and 5 – "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration of between 0.01μM and 1M, and preferably between 0.1μM and 10mM." *See* Claim 18.
34. A composition according to claim 33, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-4}% to 1% by weight relative to the total weight of the composition.	Pages 4 and 5 – "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration of between 0.01μM and 1M, and preferably between 0.1μM and 10mM." *See* Claim 18.
35. A composition according to claim 31, wherein said at least one cosmetic or	Page 5 – "Thus even the products which are considered to be inert in a cosmetic or

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
pharmaceutical product is a preservative, a surfactant, a perfume, a solvent, or a propellent.	pharmaceutical, more particularly dermatological, composition may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, such as in particular preservatives, surfactants, perfumes, solvents or propellants." *See* Claim 21.
36. A composition according to claim 35, wherein said at least one cosmetic or pharmaceutical product is a sunscreen, an α-hydroxy acid, a β-hydroxy acid, an α-keto acid, a β-keto acid, a retinoid, an anthralin, an anthranoid, a peroxide, minoxidil or one of its derivatives, a lithium salt, an antiproliferative agent, vitamin D or one of its derivatives, vitamin B9 or one of its derivatives, a hair dye, a hair colorant, capsaicin, a perfuming alcoholic solution, an antiperspirant, a depilatory waving active agent, a permanent waving active agent, a depigmenting agent, an antilouse active agent, a detergent, or a propigmenting agent.	Pages 5 and 6 – "Accordingly, products considered as active agents in cosmetic or pharmaceutical compositions may exhibit an irritant character . . . such as especially some sunscreens, α-hydroxy acids . . . β-hydroxy acids . . . α-keto acids, β-keto acids, retinoids . . . anthralins . . . anthranoids . . . peroxides . . . minoxidil and its derivatives . . . lithium salts, antiproliferative agents . . . vitamin D and its derivatives, hair dyes or colorants . . . perfuming alcoholic solutions, antiperspirants . . . depilatory or permanent waving active agents, depigmenting agents . . . capsaicin . . . antilouse active agents . . . ionic and nonionic detergent agents and propigmenting agents." *See* Claim 22.
37. A composition according to claim 36, wherein said β-hydroxy acid is salicylic acid or one of its derivatives.	Page 5 – "β-hydroxy acids (salicylic acid and its derivatives) . . . ." *See* Claim 22.
38. A composition according to claim 36, wherein said at least one cosmetic or pharmaceutical product is a retinoid.	Page 6 – "Among these products with a secondary irritant effect, the invention relates more particularly to retinoids." *See* Claim 23.
40. A composition according to claim	Page 6 – "Among the vitamin D and its

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
36, wherein said vitamin D or one of its derivatives is vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3, calcipotriol, 1,24-diOH vitamin D_3, 24,25-diOH vitamin D_3, 1-OH vitamin D_2, or 1,24-diOH vitamin D_2.	derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2." *See* Claim 25.
41. A composition according to claim 40, wherein said 1,24-diOH vitamin D_3 is tacalcitol.	Page 6 – "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2." *See* Claim 25.
42. A composition according to claim 37, wherein said salicylic acid derivative is 5-n-octanoylsalicylic acid, 5-n-dodecanoylsalicylic acid, or one of their esters.	Pages 6 and 7 – "Among the salicylic derivatives, there may be mentioned more particularly 5-n-octanoylsalicylic acid and 5-n-dodecanoylsalicylic acid or their esters." *See* Claim 26.
45. A composition according to claim 43, wherein said at least one nitric oxide synthase inhibitor is N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, N^G-amino-L-arginine, or N^G,N^G-dimethylarginine.	Page 7 – "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen." *See* Claim 27.
46. A composition according to claim	Page 7 – "Among these NO-synthase

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
45, wherein said at least one nitric oxide synthase inhibitor is the methyl ester of N^G-nitro-L-arginine, N^G,N^G-dimethylarginine, N^G-nitro-L-arginine or N^G-monomethyl-L-arginine.	inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen." *See* Claim 27.
47. A composition according to claim 31, wherein said composition is formulated in order to be applied topically to the skin, the scalp, or the mucous membranes.	Page 8 – "By the local route, the topical route is preferred, that is to say by direct application to the skin, the scalp, the nails or the mucous membranes." *See* Claim 30.
48. A method of reducing the cutaneous irritant effect of a topically applied cosmetic or pharmaceutical composition containing at least one cosmetic or pharmaceutical product capable of having an irritant character on the skin, the scalp, the nails, or the mucous membranes, said method comprising applying said cosmetic or pharmaceutical product to said skin, scalp, nails, or mucous membranes, wherein said cosmetic or pharmaceutical composition further comprises at least one nitric oxide synthase inhibitor in an amount effective to reduce the cutaneous irritant effect of said at least one cosmetic or pharmaceutical product.	Page 3 – "Thus, the subject of the present invention is a process for decreasing the cutaneous irritant effect of at least one product applied topically to the skin, the scalp, the nails or the mucous membranes and used in the cosmetic or pharmaceutical, more particularly dermatological, field, characterized in that an effective quantity of at least one NO-synthase inhibitor is used." *See* Claim 1.
49. A method according to claim 48, wherein said at least one nitric oxide synthase inhibitor is present in a	Pages 4 and 5 – "However, by way of illustration, a composition according to the invention comprises in general at least one

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
concentration ranging from 10^{-6}% to 10% by weight relative to the total weight of the composition.	NO-synthase inhibitor at a concentration of between 0.01µM and 1M, and preferably between 0.1µM and 10mM." *See* Claim 18.
50. A method according to claim 49, wherein said at least one nitric oxide synthase inhibitor is present in a concentration ranging from 10^{-4}% to 1% by weight relative to the total weight of the composition.	Pages 4 and 5 – "However, by way of illustration, a composition according to the invention comprises in general at least one NO-synthase inhibitor at a concentration of between 0.01µM and 1M, and preferably between 0.1µM and 10mM." *See* Claim 18.
51. A method according to claim 50, wherein said at least one cosmetic or pharmaceutical product is a preservative, a surfactant, perfume, a solvent, or a propellent.	Page 5 – "Thus even the products which are considered to be inert in a cosmetic or pharmaceutical, more particularly dermatological, composition may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, such as in particular preservatives, surfactants, perfumes, solvents or propellants." *See* Claims 3 an 21.
52. A method according to claim 48, wherein said at least one cosmetic or pharmaceutical product is a sunscreen, an α-hydroxy acid, a β-hydroxy acid, an α-keto acid, a β-keto acid, a retinoid, an anthralin, an anthranoid, a peroxide, minoxidil or one of its derivatives, a lithium salt, an antiproliferative agent, vitamin D or one of its derivatives, vitamin B9 or one of its derivatives, a hair dye, a hair colorant, capsaicin, a perfuming alcoholic solution, an antiperspirant, a depilatory waving active agent, a permanent waving active agent, a depigmenting agent, an antilouse active agent, a detergent, or a propigmenting agent.	Pages 5 and 6 – "Accordingly, products considered as active agents in cosmetic or pharmaceutical compositions may exhibit an irritant character . . . such as especially some sunscreens, α-hydroxy acids . . . β-hydroxy acids . . . α-keto acids, β-keto acids, retinoids . . . anthralins . . . anthranoids . . . peroxides . . . minoxidil and its derivatives . . . lithium salts, antiproliferative agents . . . vitamin D and its derivatives, hair dyes or colorants . . . perfuming alcoholic solutions . . . antiperspirants . . . depilatory or permanent waving active agents . . . depigmenting agents . . . capsaicin . . . antilouse active agents . . . ionic and

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
	nonionic detergent agents and propigmenting agents." *See* Claims 4 and 22.
53. A method according to claim 52, wherein said β-hydroxy acid is salicylic acid or one of its derivatives.	Page 5 – "β-hydroxy acids (salicylic acid and its derivatives) . . . ." *See* Claims 4 and 22.
54. A method according to claim 52, wherein said at least one cosmetic or pharmaceutical product is a retinoid.	Page 6 – "Among these products with a secondary irritant effect, the invention relates more particularly to retinoids." *See* Claims 5 and 23.
56. A method according to claim 52, wherein said vitamin D or one of its derivatives is vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3, calcipotriol, 1,24-diOH vitamin D_3, 24,25-diOH vitamin D_3, 1-OH vitamin D_2, or 1,24-diOH vitamin D_2.	Page 6 – "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2." *See* Claims 7 and 25.
57. A method according to claim 56, wherein said 1,24-diOH vitamin D_3 is tacalcitol.	Page 6 – "Among the vitamin D and its derivatives there may be mentioned more particularly vitamin D_3, vitamin D_2, 1,25-diOH vitamin D_3 (calcitriol), calcipotriol, 1,24-diOH vitamin D_3 (such as tacalcitol), 24,25-diOH vitamin D_3, 1-OH vitamin D2, 1,24-diOH vitamin D_2." *See* Claims 7 and 25.
58. A method according to claim 53, wherein said salicylic acid derivative is 5-n-octanoylsalicylic acid, 5-n-dodecanoylsalicylic acid, or one of their esters.	Pages 6 and 7 – "Among the salicylic derivatives, there may be mentioned more particularly 5-n-octanoylsalicylic acid and 5-n-dodecanoylsalicylic acid or their esters."

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
	See Claims 8 and 26.
61. A method according to claim 59, wherein said at least one nitric oxide synthase inhibitor of N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, N^G-amino-L-arginine, or N^G,N^G-dimethylarginine.	Page 7 – "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen." *See* Claims 9 and 27.
62. A method according to claim 61, wherein said at least one nitric oxide synthase inhibitor is the methyl ester of N^G-nitro-L-arginine, N^G,N^G-dimethylarginine, N^G-nitro-L-arginine, or N^G-monomethyl-L-arginine.	Page 7 – "Among these NO-synthase inhibitors, there may be mentioned in particular N^G-monomethyl-L-arginine, the methyl ester of N^G-nitro-L-arginine, N^G-nitro-L-arginine, diphenyleneiodonium chloride, 7-niro-indazole, N(5)-(1-iminoethyl)-L-ornithine, [2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazolin-1-oxyl]-3-oxide, N^G,N^G-dimethyl-L-arginine, N^G,N^G-dimethylarginine, aminoguanidine, canavanine and ebselen." *See* Claims 9 and 27.
63. A process for the cosmetic treatment of the skin, the scalp, the nails, or the mucous membranes, said process comprising applying a cosmetic composition according to Claim 31 to said skin, scalp, nails, or mucous membranes.	Page 4 – "The present invention also relates to a process of cosmetic treatment, characterized in that it uses the cosmetic composition according to the invention." Page 8 – "By the local route, the topical route is preferred, that is to say by direct application to the skin, the scalp, the nails or the mucous membranes."

Claim	Disclosure in the English Translation of the French Priority Document, French National Registration No. 95/02,267
	See Claims 15 and 30.
64. A process for the pharmaceutical treatment of the skin, the scalp, the nails, or the mucous membranes, said process comprising applying a pharmaceutical composition according to Claim 31 to said skin, scalp, nails, or mucous membranes.	Page 4 – "The present invention also relates to a process of cosmetic treatment, characterized in that it uses the cosmetic composition according to the invention." Page 8 – "By the local route, the topical route is preferred, that is to say by direct application to the skin, the scalp, the nails or the mucous membranes." *See* Claims 15 and 30.
65. A composition according to claim 38, wherein said retinoid is all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester.	Page 6 – "Among the retinoids, there may be mentioned more particularly all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester . . . ." *See* Claim 24.
66. A method according to claim 54, wherein said retinoid is all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester.	Page 6 – "Among the retinoids, there may be mentioned more particularly all-trans-retinoic acid, 13-cis-retinoic acid, 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid, or 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester . . . ." *See* Claim 24.

Accordingly, the '990 and the '003 patent are not prior art to at least claims 31-42, 45-50, and 61-66 for this additional reason. With regard to dependent claims 43, 44, 59, and 60, Applicant does not believe the '990 and the '003 patent are prior art. However, Applicant also notes that the '990 and the '003 patent fail to teach and/or suggest that the nitric oxide synthase inhibitor is an inhibitor of constitutive nitric oxide synthase or that the inhibitor of constitutive nitric oxide synthase is an inhibitor of endothelial nitric oxide synthase. *See* the '990 patent at Col. 8, ll. 44-58; the '003 patent at Col. 9, ll. 40-53. As such, even if the '990 or the '003 patent was cited against the present application, the '990 or the '003 patent fail to teach all the elements of claims 43, 44, 59, and 60, and thus, do not anticipate and/or render obvious claims 43, 44, 59, and 60. *See* M.P.E.P. §§ 2131, 2143 (8th ed. Rev. 2, 2004).

Finally, the rejection of pending claims over the '688 patent in view of either the '990 patent or the '003 patent fails in a similar manner. Without the '990 or the '003 patent, the '688 patent's teachings are woefully deficient. For example, the Office acknowledges that "'688 [patent] do[es] not specifically teach the inhibitor compounds as anti-irritants together with the composition. '688 [patent] teach[es] topical application as transdermal patches but do[es] not teach the composition in the form of gel or cream." Office Action at page 4. Thus, by the Office's own admission, the '688 patent cannot establish a *prima facie* case of obviousness alone and thus, Applicant respectfully requests the withdrawal of the rejection for at least the reasons identified above.

Applicant therefore respectfully request that the application be passed to allowance for these additional reasons.

III. Conclusion

Accordingly, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

If the Examiner believes that a telephone conference call could be useful in resolving any outstanding issues, she is respectfully urged to contact Applicant's undersigned counsel at 202.408.4345.

Please grant any extensions of time required to enter this paper and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 21, 2005

By: _____
Adriana L. Burgy
Reg. No. 48,564

Attachment: Certified English Translation of French Application No. 95/02,267